**REMARKS**

This amendment is in response to the Official Action issued July 1, 2003 in connection with the above-identified application. Claim 6 has been cancelled and new Claim 23 has been added. Claims 1, 11 and 23 are now pending in the application. Claim 1 has been amended herein as is further discussed below. No new matter has been introduced by virtue of the amendments made herein, as is further discussed below. This amendment is also in response to the Notice of Non-Compliant Amendment mailed July 24, 2003. In response to the Notice, Claims 2-3, 5, 7-10 and 12-22, previously identified as "Withdrawn", have been identified as "Cancelled."

Claims 1, 6 and 11 have been rejected under 35 U.S.C. 112, first paragraph, as allegedly not enabled. In particular, the Examiner has alleged that the invention as claimed in Claim 1 cannot be practiced without undue experimentation. *See* Official Action, page 7, lines 7-13 and p. 3, lines 14-15.

In response, Claim 1 has been amended, without prejudice and in the interest of facilitating prosecution, to recite the limitations of now canceled Claim 6, *i.e.,* that the drug for which the major clearance mechanism in humans is CYP2D6 mediated oxidative biotransformation is (2S,3S)-2-phenyl-3-(2-methoxy-5-trifluoromethoxyphenyl) methylamino-piperidine, or a pharmaceutically acceptable salt thereof. It is respectfully submitted that the amendment to Claim 1 is supported by the specification as originally filed, for example, on p. 6, lines 15-19, and therefore does not constitute new matter. Furthermore, it is respectfully submitted that no undue experimentation would be required by a person of ordinary skill in the art to practice the invention of Claim 1 in light of the foregoing amendment, and that Claim 1 as amended is accordingly enabled within the meaning of 35 U.S.C. 112, first paragraph. Claim 11 further limits Claim 1 and is therefore likewise enabled.

In view of the foregoing, withdrawal of the rejection under 35 U.S.C. 112, first paragraph of Claims 1 and 11 as allegedly not enabled is respectfully requested.

Claims 1, 6 and 11 have been rejected under 35 U.S.C. 103(a) as allegedly obvious over Benet et al. (U.S. Patent No. 5,567,592) and Hess (WO 96/14845). In particular, the Examiner has stated that Benet et al. teaches the administration of a drug that is a CYP2D6 substrate, and that CYP2D^ inhibitors such as quinidine, calcium channel blockers, and phenothiazinies are useful as bioenhancers of pharmaceutical compounds. *See* Official Action, p. 8, lines 4-9. The Examiner has further stated that Hess discloses that (2S,3S)-2-phenyl-3-(2-methoxy-5-trifluoromethoxyphenyl)methylamino-piperidine is an NK-1 receptor antagonist. *See* Official Action, p. 8, lines 13-15. The Examiner has concluded that it would have been obvious to combine the teachings of Benet et al. with the teachings of Hess in light of the holding in *In re Kerkhoeven,* 205 USPQ 1069 (CCPA 1980) to obtain the present invention. *See* Official Action, p. 10, lines 14-15.

Applicants respectfully traverse. The combined use of a CYP2D6 inhibitor with (2S,3S)-2-phenyl-3-(2-methoxy-5-trifluoromethoxyphenyl)methylamino-piperidine is not obvious in view of the cited reference. Obviousness requires a motivation or suggestion to combine the teachings of the prior art references. However, there is no motivation or suggestion in the cited references to combine the teachings to obtain the present invention. Moreover, the Examiner's statements with regard to other enzymes, such as CYP3A, are not applicable to a specific class of drugs, as noted in the amendment filed on February 7, 2002, and certainly not to a specific drug such as (2S,3S)-2-phenyl-3-(2-methoxy-5-trifluoromethoxyphenyl)methylamino-piperidine. Furthermore, the Examiner's reliance on *In re Kerkhoeven* is misplaced. *In re Kerkhoeven* is applicable to the case where two compositions, "each of which is taught by the prior art to be useful for the same purpose," are used to form a third composition which is to be used for the very same purpose. 205 USPQ at 1072. In *In re Kerkhoeven,* the claims required the mixing together of two conventional spray-dried detergents, each of which had the same purpose. *In re Kerkhoeven* does not apply where the two components of a composition each have a different purpose. *See Ex parte Bokisa,* 1997 WL 1897871, *3+ (Bd. Pat. App & Interf. Apr 10, 1997). In contrast, in Claim 1 of the present application, the first component, (2S,3S)-2-phenyl-3-(2-methoxy-5-trifluoromethoxyphenyl)methylamino-piperidine, is an NK-1 receptor antagonist. The second component is instead a CYP2D6 inhibitor and therefore has the purpose of inhibiting the CYP2D6 enzyme. The two components therefore do not have the same purpose. Thus, the factual pattern in the instant case is distinguishable from *In re Kerkhoeven*, and therefore *In re Kerkhoeven* is not applicable to this case.

Accordingly, there can be no assertion of obviousness in the absence of a motivation or suggestion to combine the teachings of the prior art references to obtain the invention of Claim 1. Claim 11 further limits the invention of Claim 1 and is therefore likewise non-obvious over the cited references. In view of the foregoing, withdrawal of the rejection under 35 U.S.C. 103(a) of Claims 1 and 11 as allegedly obvious over Benet and Hess is respectfully requested.

New Claim 23 has been added to further claim the invention. It is respectfully submitted that new Claim 23 is supported by the specification as originally filed, for example, on p. 7, lines 31-34, and therefore does not constitute new matter. It is respectfully submitted that new Claim 23 is patentable over the cited references.

In view of the amendments and remarks made herein, applicants respectfully request reconsideration and withdrawal of the rejection set forth in the July 1, 2003 office action, and solicit the issuance of a notice of allowance. If a telephone interview is deemed to be helpful to expedite the prosecution of the subject application, the Examiner is invited to contact applicant's undersigned attorney at the telephone number provided.

The Commissioner is hereby authorized to charge any fees required under 37 C.F.R. §§1.16 and 1.17 or to credit any overpayment to Deposit Account No. 16-1445.

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